Claims

1. A process for the in vitro differentiation of neuronal stem cells and of cells derived from neuronal stem cells, comprising
   (a) contacting the cells with a substance which inhibits a reaction of the Wnt signal transduction pathway, and
   (b) culturing said cells under conditions which enable said cells to propagate and/or differentiate.

2. The process as claimed in claim 1, characterized in that the cells differentiate into brain cell-like cells.

3. The process as claimed in claim 1 or 2, characterized in that, where appropriate, a step (c) comprises determining the concentration of a protein of the Wnt signal transduction pathway.

4. The process as claimed in claim 3, characterized in that the protein concentration is determined by means of an antibody.

5. The process as claimed in claim 4, characterized in that the protein is β-catenin.

6. The process as claimed in any of claims 1 to 3, characterized in that the reaction of the Wnt signal transduction pathway is inhibited by way of inhibition of glycogen synthase kinase 3.

7. The process as claimed in claim 6, characterized in that glycogen synthase kinase 3 is inhibited by at least one inhibitor selected from the group consisting of kinase inhibitors, estrogen analogs, phytoestrogens, corticoids and salts, in particular 4-benzyl-2-methyl-1,2,4-thiazolidine-3,5-dione, 2-thio(3-iodobenzyl)-5-(1-pyridyl)-[1,3,4]-oxadiazole, 3-(2,4-dichlorophenyl)-4-(1-methyl-1H-indol-3-yl)-1H-pyrrole-2,5-dione, 3-[(3-chloro-4-hydroxyphenyl)amino]-4-(2-nitrophenyl)-1H-pyrrole-2,5-dione, lithium salts, beryllium salts.

8. The process as claimed in claim 7, characterized in that the inhibitor is genistein.

9. The process as claimed in claim 8, characterized in that genistein is used in a concentration of 10-250 μmol/l.

10. The process as claimed in any of claims 1 to 3, characterized in that the reaction of the Wnt signal transduction pathway is inhibited by at least one antagonist of the Frizzled receptor.

11. The process as claimed in claim 10, characterized in that the at least one antagonist is selected from the group consisting of secreted Frizzle-related proteins (sFRP), Dickkopf (Dkk), Wnt, Fzd, Frat, Nkd, VANG1/STB2, ARHU/WRCH1, ARHV/WRCH2, GIPC2, GIPC3, betaTRCP2/FBXW1B, SOX17, TCF-3, WIF-1, Cerberus, Sizzled, Crescent, Coco, Soggy, Kremen and low-density-lipoprotein-receptor-related proteins (LRP).

12. The process as claimed in any of claims 1 to 11, characterized in that the cells derived from neuronal stem cells are cells selected from the group consisting of neuroblastoma cells, PC12 cells, cells of neuronal primary cultures and 293 cells.

13. A cell obtainable by the process as claimed in any of claims 1 to 12.

14. A neurological tissue replacement comprising cells as claimed in claim 13.

15. A pharmaceutical agent comprising cells as claimed in claim 13.

16. A screening process for identifying substances which inhibit the Wnt signal transduction pathway and are suitable for the differentiation of neuronal stem cells and of cells derived from neuronal stem cells, comprising

(c) contacting said cells with said substance,
(d) determining the β-catenin concentration in said cells,
(e) comparison with a suitable comparative cell, and
(f) detecting differentiation of said cells.

17. A pharmaceutical agent comprising inhibitors of glycogen synthase kinase 3, antagonists of the Frizzled receptor and/or antibodies to proteins of the Wnt signal transduction pathway.

18. The agent as claimed in claim 17, characterized in that the inhibitor of glycogen synthase kinase 3 is genistein.

19. The use of a pharmaceutical agent as claimed in any of claims 15, 17 and 18 for preparing a medicament for the treatment of diseases on which modulation of the

activity or amount of a protein of the Wnt signal transduction pathway may have a beneficial influence.

20. The use as claimed in claim 19, characterized in that the disease is one selected from the following groups:
the group of cerebral malformations, in particular of cerebral developmental anomalies, cerebral palsies in infants, craniocervical junction abnormalities and dysraphic syndromes,
the group of degenerative and atrophic processes of the brain and the spinal cord, in particular of senile and presenile atrophies of the brain, in particular Alzheimer's disease, Binswanger's disease and Pick's disease,
the group of basal ganglia disorders, in particular Huntington's disease and HDL2, chorea, athetosis and dystonia, spongiform encephalopathies,
the group of degenerations of the corticospinal tract and of the anterior horn of the spinal cord, in particular amyotrophic lateral sclerosis, spinal muscular atrophy and progressive bulbar paralysis,
the group of degenerative ataxias, in particular Friedreich's disease, Refsum's disease and spinocerebellar ataxias type 1-25,
the group of metabolic and toxic processes of the brain and of the spinal cord, Wilson's disease, multiple sclerosis, demyelinating diseases of the central and peripheral nerve system, brain and spinal cord tumors, traumatic damage to the nerve system, circulation disorders of the brain and the spinal cord, in particular hereditary metabolic disorders of the amino acid, lipid, carbohydrate and metal ion metabolisms, in particular Wilson's disease, multiple sclerosis, cerebral infarctions and other forms of stroke, muscular disorders based on damage to the nerve system and post-traumatic muscular atrophies.

21. The use of genistein for preparing a medicament for the treatment of diseases which lead directly or indirectly to the death of brain cells.

22. A screening process for detecting brain cell-like cells and brain cells, comprising

(i) determining the concentration of β-catenin, and
(ii) comparing the concentration from (i) with the β-catenin concentration of a suitable comparative cell.

23. The screening process as claimed in claim 22, characterized in that the β-catenin concentration is determined by means of an antibody.

24. The use of β-catenin as diagnostic marker for identifying brain cell-like cells and brain cells.

25. An in vitro differentiation of recombinant, neuronal stem cells into brain cell-like cells, effected by a nucleic acid construct for expressing a protein capable of inhibiting a reaction of the Wnt signal transduction pathway.

26. The differentiation as claimed in claim 25, characterized in that the protein is expressed under the control of a constitutive or of a regulatable promoter.

27. The differentiation as claimed in claim 25 or 26, characterized in that the cell has been transfected stably or transiently with the nucleic acid construct.

28. A differentiation of a recombinant, neuronal stem cell into brain cell-like cells, effected by at least one protein of the Wnt signal transduction pathway not being expressed, being expressed inactively or being expressed at a reduced level in comparison with the corresponding wild type stem cell.

29. The differentiation as claimed in claim 28, characterized in that at least one gene coding for a protein of the Wnt signal transduction pathway or a DNA section involved in expression of said gene has been completely or partially deleted or has a mutation.

30. A kit for in vitro differentiation of neuronal stem cells and of cells derived from neuronal stem cells, comprising a recombinant, neuronal stem cell which comprises a nucleic acid construct for expressing a protein capable of inhibiting a reaction of the Wnt signal transduction pathway.

31. A kit for in vitro differentiation of neuronal stem cells and of cells derived from neuronal stem cells, comprising a recombinant, neuronal stem cell in which at least one protein of the Wnt signal transduction pathway is not expressed, is expressed inactively or is expressed at a reduced level in comparison with the corresponding wild type stem cell.